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PATENT
Attorney Docket No.: JHU1680-2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Germino et al.	Art Unit:	1634
Application No.:	09/904,968	Examiner:	S. Sakelaris
Filed:	July 13, 2001		
Title:	DETECTION AND TREATMENT OF POLYCYSTIC KIDNEY DISEASE		

Commissioner for Patents
Washington, D.C. 20231

TRANSMITTAL SHEET

Transmitted herewith for the above-identified application please find:

1. Response to Restriction Requirement (6 pages);

2. Return receipt postcard.

CERTIFICATION UNDER 37 CFR §1.8
I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service as first class mail on this date, **March 6, 2003**, in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231.
Cara Grifone *(Name of Person Mailing Paper)*
Cara Grifone **March 6, 2003** *(Signature)* *(Date)*

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No fee is deemed necessary in connection with the filing of this Response. However, if any fee is required, authorization is hereby given to charge Deposit Account No. 50-1355.

Respectfully submitted,

Date: March 6, 2003

Lisa A. Haile, J.D., Ph.D.
Registration No. 38,347
Telephone: (858) 677-1456
Facsimile: (858) 677-1465

USPTO CUSTOMER NUMBER 28213
GRAY CARY WARE & FREIDENRICH LLP
4365 Executive Drive, Suite 1100
San Diego, CA 92121-2133

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RESPONSE TO RESTRICTION REQUIREMENT

Sir:

This Reply is being filed in response to the Action mailed February 4, 2003, Paper No. 16. The Examiner asserts that the Applicants were non-responsive in the reply filed on November 26, 2002 for failing to elect the specific mutation detected by the elected method. This is not understood. Applicants elected the precise example of a suitable election, employing almost identical language as the Examiner in the sentence bridging pages 3-4 of Paper Number 10. In response to this new restriction requirement, Applicants elect the mutation wherein nt3110 is a C with traverse.

The requirement is being traversed for the reasons set forth in detail in the prior response and below.

CERTIFICATION UNDER 37 CFR §1.8

I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service as first class mail on this date, **March 6, 2003,** in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231.

Cara Grifone
(Name of Person Mailing Paper)

(Signature) **March 6, 2003** *(Date)*

The Invention

The present invention relates generally to the diagnosis and treatment of polycystic kidney disease and more specifically to probes and agents useful in diagnosis and treatment of polycystic kidney disease and related disorders. The present invention provides oligonucleotide primers for the polymerase chain reaction (PCR) that selectively amplify regions of a PKD1 gene, but not its homologs and further provides oligonucleotide primers for nested PCR directed at selective amplification of regions of a PKD1 gene. The present invention further discloses methods for detection a wild type and mutant PKD1 gene and methods for identifying mutations within a PKD1 gene as well as its amplified regions. Additionally, the present invention relates to kits that utilize agents and methods of the present invention. The present invention also provides vectors and host cells containing the above-identified agents.

The Restriction Requirement

The restriction, as articulated in Paper No. 10, sets forth 44 different Groups of inventions. Inventions in Groups 1- 43 comprise the subject matter that is defined by the Claims 1-66 as filed as well as Claims 68-75. Group 44 encompasses subject matter defined by Claim 67. The instant traversal is limited to Groups 1-43 for which recombination is requested.

The Examiner states that Groups 1- 43 include inventions that are patentably distinct in structure and physiochemical properties because they are each drawn to different nucleic acid sequences. The Examiner does not provide the details of which sequences belong to each of the 43 Groups. The Examiner further states that the compositions are utilized in different methodologies, e.g. such as in hybridization to different regions of the same gene, and that no Group requires the invention of the other, since each invention has different primary sequence.

It appears that a further restriction is applied. The Examiner states that "the Applicant must elect a single primer pair from nucleic acid sequence SEQ ID NOS: 3-18, a single nested primer pair that corresponds to the elected primer pair consisting of SEQ ID NOS: 19-50, 51 and 61 and SEQ ID NOS: 62 to 92, 113, and 97 to 112, and a single polynucleotide region containing a mutation as specified in Claim 20 that is detected specifically by the elected primer pair and nested primer pair." (Page 3, last paragraph.) The Applicant is advised that examination will be restricted to only the elected SEQ ID NOS. and that such sequence election requirement should not be construed as species election. The Examiner appears to imply that the generic invention will not be examined.

In Paper No. 16, the Examiner restricts even further within the claim. Even though the elected primer pairs will detect the four mutations explicitly acknowledged by the Examiner, the Examiner is restricting Applicants to a single mutation to be detected.

Groups 1- 43 should be rejoined

Under the decision of *In re Weber*, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 198 USPQ 334 (CCPA 1978), it is improper for the Patent Office to refuse to examine that which applicants regard as their invention unless it lacks unity of invention. (MPEP 803.02.) Unity of invention exists where the compounds share a common utility and a substantial structural relationship, disclosed as being essential to that utility.

Nucleic acid sequences of Groups 1- 43 all share a common utility, namely, they comprise primers useful for selectively amplifying a region of a PKD1 gene, but not a corresponding region of a PKD1 homolog. Also provided are nested primer pairs useful for performing nested amplification of a PKD1-specific amplification product of a PKD1 gene. Therefore the nested primers also share the common utility of the nucleic acid sequences of Groups 1- 43. The elected primer pairs also share the common utility of detecting mutations (or the absence of a mutation) within the same fragment of the nucleotide sample.

Nucleic acid sequences of Groups 1- 43 all share a structural feature disclosed as being essential to the above specified utility. Specifically, the primers are all polynucleotides with

sequences that specifically hybridize to a PKD1 gene. As in *In re Weber* and *In re Haas*, the mere fact that the members of the claimed genus are not identical in chemical structure does not destroy the fact that all members of the genus have a substantial common core structure.

The Examiner states that, since each species of nucleic acid may encode a different polypeptide with distinct biochemical and physical properties, each nucleic acid acquires a separate status in the art and results in a search that is not coextensive in scope. It is noted that the courts and statutes do not contemplate defining the burden of search to justify a restriction requirement as being a requirement that the search be "coextensive in scope." Certainly, that was not the case in *Weber* and *Haas*, which presented the office with claims to a genus of multiple species subject to a different search. That is certainly not the test applied in MPEP 803.02 which clearly contemplates the examination of structurally related (not identical) species which do not share a coextensive search. Likewise, identity in physical and biochemical properties is not required by this jurisprudence to present claims drawn to multiple embodiments in a single application. Thus, the Examiner's position is clearly not well founded in the law.

Furthermore, the Examiner's reference to various nucleic acids as encoding different proteins misses the invention scientifically. The invention relates to diagnostic methods of identifying the composition? structure? of a PKD1 gene sequence in a sample, the products useful in such methods (e.g. primers, primer pairs, nested primer pairs), and kits containing such products. Any search by the examiner of proteins encoded by primers will not be expected to identify the most relevant art. The most relevant search will likely be of the gene sequence sought to be detected, i.e. that of PKD1 gene.

According to the Opinion of *In re Weber*, 198 USPQ 328 (CCPA 1978), third paragraph:

> As a general proposition, an applicant has a right to have *each* claim examined on the merits. If an applicant submits a number of claims, it may well be that pursuant to a proper restriction requirement, those claims will be dispersed to a number of applications. Such action would not affect the right of the applicant eventually to have each of the claims examined in the form he considers to best

define his invention. If, however a single claim is required to be divided up and presented in several applications, that claim would never be considered on its merits.

Claims of the Groups 1 - 43 comprise generic claims drawn to the use of nucleotide sequences that share a common utility and a substantial structural relationship and that define the Applicant's invention. Restricting the species of these generic claims to very specific pair combinations in multiple applications will ensure that the generic invention will never be considered on its merits.

Furthermore, the sheer number of the Groups of invention set forth by the Examiner all but precludes the Applicant from exercising his rights to having each claim examined on the merits. The precise number of inventions identified is unclear from the structure of the restriction requirement. There may be 44 inventions requiring 44 applications. The failure to provide reasonable direction in the restriction leaves open a possibility that each and every sequence, pair of sequences and nested pairs requires its own application. In light of this new restriction requirement, which infers that, even with regard to the specific elected primer, primer pair or nested primer pair, the search will be limited to only one specific mutation that can be identified by the use of the elected primer(s), the number of applications required by this Examiner is much greater than 44. In this case, the number of applications becomes exceedingly high. The burden of filing 44 or more different applications within a claim is tantamount to a rejection of that claim and a refusal to examine the Applicants' invention.

The ambiguous structure of the restriction requirement further precludes the Applicant from presenting meaningful claims commensurate with the elected species, as envisioned by the Examiner or in determining the scope of claims that can be pursued in a divisional application enjoying the protections afforded by 35 USC 121.

Applicants therefore again request that the three restriction requirements be withdrawn and replaced with requirements for election of species (i.e., SEQ ID NOS.). Applicants request further that the elected species be examined, and, upon a finding that the elected species is allowable, that the entire scope of the claims be examined. Applicants hereby elect primers SEQ

ID NOS: 3 and 4, nested primer pair SEQ ID NOS: 19 and 20, polynucleotides containing PDK1 mutations located in regions amplified by said nested primers, the methods of detecting this specific region with these specific nested primer pairs and kits containing these same primer pairs to amplify said specific region. The specific, elected mutation which can be identified by the elected method is the mutation wherein nt 3110 is a C.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (858) 677-1456.

Respectfully submitted,

Date: March 6, 2003

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